7200 Lake Ellenor Dr.
Suite 252
Orlando, Florida 32809
USA

Van Dyke & Associates, PA
INTELLECTUAL PROPERTY LAW

Phone: (407) 240-0085
Toll Free: (888) 416-1464
Fax: (407) 240-1007
info@patentinternational.com
www.patentinternational.com

FACSIMILE COVER SHEET

TO	:	Examiner Richard Schnizer
COMPANY	:	USPTO
FAX No.	:	703 308 4242
No of PAGES	:	6 (including cover sheet)
FROM	:	Timothy H. Van Dyke
DATE	:	September 3, 2003
RE	:	Serial No. 09/360,199

SENT VIA FACSIMILE ONLY

Please Deliver to Examiner Schnizer immediately.

Examiner Schnizer:

I attach for your consideration a Second Declaration of Jack Gauldie. This Declaration further addresses the issues set forth in the latest office action dated February 26, 2003.

A Notice of Appeal was filed in the subject application on July 28, 2003. Applicant requests a telephonic interview with the Examiner to discuss the data provided in the Second Declaration and to discuss pending issues. The undersigned will be contacting you within the next few days to schedule such interview.

Should you have any questions, please contact the undersigned at the contact information provided at the head of this coversheet.

Respectfully submitted,

Timothy H. Van Dyke

If you do not receive all pages or if any portion of this transmission is not legible, call the sender at (407) 240-0085.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner	:	Schnizer, Richard
Art Unit	:	1635
Applicants	:	Gauldie et al.
Serial No.	:	09/360,199
Docket No.	:	GDI-1CPA1
Filed	:	07/23/1999
For	:	Intestinal Gene Therapy

Assistant Commissioner for Patents
Washington, D.C. 20231

SECOND DECLARATION OF JACK GAULDIE, PhD.

I Jack Gauldie, Ph.D. hereby declare and say as follows:

THAT, I am employed as Professor and Chairman, Department of Pathology at McMaster University, Hamilton, Ontario, Canada.;

THAT, I earned my Ph.D. in Biological Chemistry in 1968, from University College, University of London UK;

THAT, I am one of the above-named Applicants and inventors of the subject matter described and claimed in the above-identified patent application;

THAT, by virtue of my educational and employment background, my attendance at seminars, my ongoing research, my continuing review of scientific periodicals and journals, and through correspondence with professional colleagues, I am aware of the level of skill of one ordinarily skilled in the art of immunology and vaccinology;

THAT, I have studied the application Serial No. 09/360,199 and all office actions which have been issued during prosecution of this application (including cited

references), as well as all responses which have been filed on the Applicants' behalf, and being thus duly qualified declare as follows:

1. In the telephonic interview with the Examiner on June 23, 2003, the Examiner questioned the ability of the techniques as described in the subject application and shown to immunize mice against herpes simplex virus HSV to also immunize higher mammals. In particular, the Examiner cited to references in the area of gene therapy and vaccination using naked DNA to support the proposition that immunization using the claimed adenoviral vector system through a mucosal route is unpredictable.[1] Thus, the Examiner opines that the protection conferred to mice is not translatable to other animals. I provide as Attachment A a summary of data obtained from three separate studies utilizing the same adenoviral vector to immunize mice, dogs and humans. This data directly addresses the Examiner's stated concern that the immunization methods as claimed would not likely work in other animals without undue experimentation.

2. The studies evaluated the ability of activating cytotoxic T-cells against human gp100, a protein prominent in melanocytes and recognized as a tumor antigen for melanoma, by administering an adenoviral vector expressing this protein. First, the adenoviral vector was used to immunize mice. The immunized mice demonstrated activation of cytotoxic T-cells as evidenced by a standard CTL assay. Second, the same adenoviral vector was administered to dogs. The treated dogs showed a quantitative increase in cytotoxic T cells specific to the human gp100 protein. See Figure 3 on page 1. Lastly, the same vector used in the mice and dog studies was administered to humans. As observed in both the mice and dog experiments, cytotoxic T-cells specific to the human gp100 were activated in humans. See the figure under paragraph 3.

3. The three studies summarized in Attachment A demonstrate that the successful immunization in mice against a specific antigen, utilizing an adenoviral vector expressing said antigen, would be expected to correlate with similar results in higher animals. In other words, when utilizing an adenoviral vector system shown to succesfully express an

[1] On this point, it is my opinion that the references the Examiner relies on are inapposite to the claimed invention and are not a reasonable and fair indicator of the likelihood of the claimed invention successfully immunizing animals other than mice.

antigen in a mouse, and which has been shown to confer protection against the pathogen from which the protein is derived, one skilled in the art would expect that the same adenoviral vector system to produce similar immunity in higher animals. We have previously submitted evidence confirming the successful immunization against HSV in mice. See first Gauldie Declaration, November 8, 2003. There is no scientific reason to doubt that the protection against HSV conferred to mice, utilizing the methods as claimed, would also confer similar protection to dogs and even humans.

4. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information in belief are believed to be true; and further that these statements were made with the knowledge that willful false statements in the like so made are punishable by fine or imprisonment, or both, under §1001 of title 18 of the U.S.C. and that such willful false statements made jeopardize the validity of the application or of any patent issuing thereon.

Further declarant sayeth naught.

Jack Gauldie

Jack Gauldie, Ph.D.

July 28, 2003

Date

ATTACHMENT A

Mouse to dog to human Jack Gauldie PhD FRSC July17, 2003

Our own experiences with immunization using gene based vaccines and the development of Cytotoxic T cells (CTL) or Interferon ϑ(IFNϑ) secreting T cells specific for the antigen.

1 We have immunized **mice** with a recombinant Adenovirus vector expressing human gp100 (a glycoprotein prominent in melanocytes and recognized as a tumor antigen for melanoma) and showed the development of Cytotoxic T cells in the spleen reactive to gp100 using a standard CTL assay (Reference - Wan Y, Emtage P, Zhu Q, Foley R, Pilon A, Roberts B, Gauldie J. Enhanced Immune Response to the Melanoma Antigen gp100 Using Recombinant Adenovirus-Transduced Dendritic Cells. Cellular Immunology 198:131-138 (1999).

2 We have used the same vector expressing the same human gp100 gene to vaccinate **dogs**, either control dogs or dogs with melanoma and showed a similar development of CTL T cells in the circulation using a standard CTL assay (Reference - Gyorffy S, Woods JP, Foley R, Kruth S, Liaw PCW, Gauldie J. Bone Marrow derived Dendritic cell Vaccination of spontaneous Canine Melanoma using Human gp100 Antigen. Submitted to Vet Immunol Immunopathol 2003.
Figure of sample CTL activity is included :

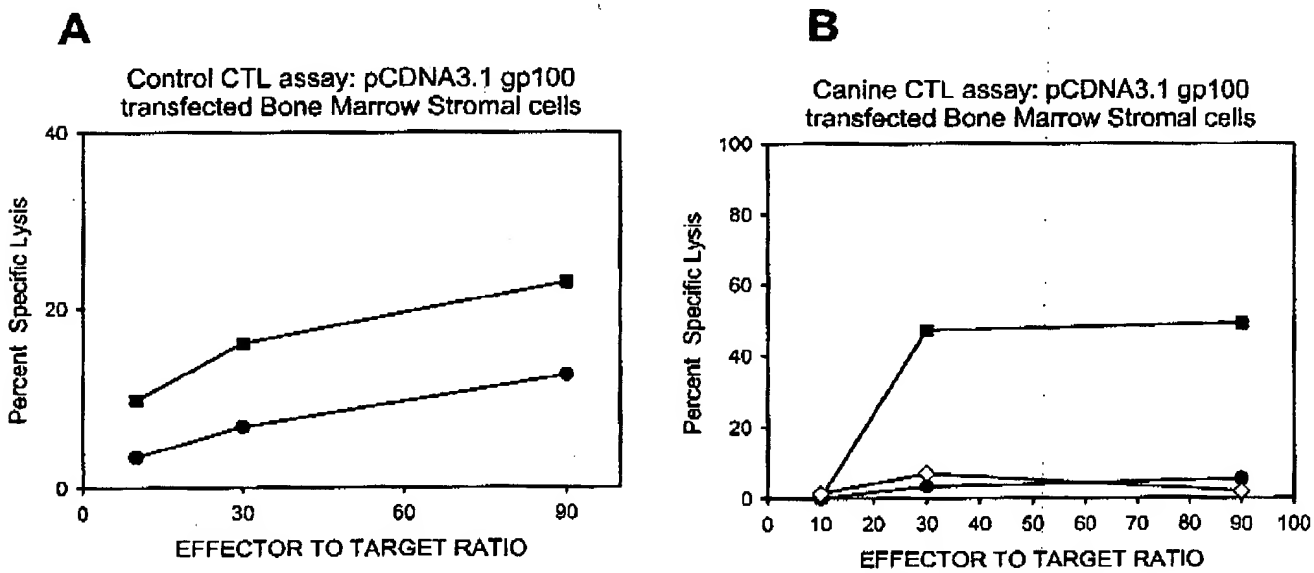

Figure 3. Peripheral blood mononuclear cells were isolated from control (left) and tumor (right) animals. Target cells were autologous stromal cells pulsed with a plasmid expressing human gp100. CTL assay carried out under standard conditions. Both dogs developed gp100 specific T cell killing after immunization.

3 We have used the same Adenovirus vector expressing human gp100 to immunize **human** clinical patients using a similar immunization protocol in a clinical trial in metastatic melanoma. Some patients have shown the development of T cells in the peripheral blood that react to gp100 and secrete IFNγ, a surrogate evaluation of CTL. This trial is still underway and has not yet been published, but the data have been presented on several occasions to peer groups at national and international meetings

Figure of sample CTL activity in the human is included: Peripheral blood mononuclear cells are recovered from patient after immunization and incubated with human gp100 expressing cells. CD8 T cells that recognize the antigen express IFNγ and are detected by FACS analysis. Patient expressed 1.70% of CD8 T cells that secrete IFNγ on exposure to gp100 antigen. Positive for CTL.

Intracellular CD8+ IFNγ Secretion Assay